In the specification:

On page 1, between the title and the heading "Field of the Invention," insert the following cross-reference to prior applications:

This application is a divisional of application Serial No. 10/285,743, filed November 1, 2002, now Patent No. 6,670,359, which is a divisional of application Serial No. 09/171,570, filed October 21, 1998, now Patent No. 6,479,497, which was the National Stage of International application No. PCT/SE98/01603, filed September 9, 1998.

On page 2, replace the paragraph running from line 6 through line 14 with the following amended paragraph:

The 5-HT Receptors

The various effects of 5-HT may be related to the fact that serotoninergic neurons stimulate the secretion of several hormones, e.g. cortisol, prolactin, β-endorphin, vasopressin and others. The secretion of each of these other hormones appears to be regulated on a specific basis by several different 5-HT (serotonin) receptor subtypes. With the aid of molecular biology techniques, to date these receptors have been classified as 5-HT_1, 5-HT_2, 5-HT_3, 5-HT_4, 5-HT_5, 5-HT_6 and 5-HT_7 with the 5-HT_1 receptor further divided into the 5-HT_{1A}, 5-HT_{1B}, 5-HT_{1D}, 5-HT_{1E} and

5-HT_{1F} subtypes. Each receptor subtype is involved in a different serotonin function and has different properties.

On page 2, replace the paragraph running from line 16 through line 25 with the following amended paragraph:

Regulation of the 5-HT transmission

The release of 5-HT is feedback-regulated by two different subtypes of 5-HT receptors. Inhibitory 5-HT_{1A} autoreceptors are located on the cell bodies in the raphé nuclei which upon stimulation by 5-HT decrease the impulse propagation in the 5-HT neurons and thereby ~~reducing~~ reduce the 5-HT released at the nerve terminals. Another subtype of inhibitory 5-HT receptors is located on the 5-HT nerve terminals, the h5-HT_{1B} receptors (in rodents the r5-HT_{1B} receptors) which regulate the synaptic concentration of 5-HT by controlling the amount of 5-HT that is released. An antagonist of these terminal autoreceptors thus increases the amount of 5-HT released by nerve impulses which has been shown in both *in vitro* and *in vivo* experiments.

On page 12, replace the paragraph running from line 8 through line 16 with the following amended paragraph:

Dosage units for rectal application can be solutions or suspensions or can be prepared in the form of suppositories

comprising the active substance in a mixture with a neutral fatty base, or gelatine rectal capsules comprising the active substance in admixture with vegetable oil or paraffin oil. Liquid preparations for oral application may be in the form of syrups or suspensions, for example solutions containing from about 0.1% to about 20% by weight of the active substance herein described, the balance being sugar and a mixture of ethanol, water, glycerol and propylene glycol. Optionally such liquid preparations may contain colouring agents, flavouring agents, ~~saccharine~~ saccharin and carboxymethyl-cellulose as a thickening agent or other excipients known to the person skilled in the art.

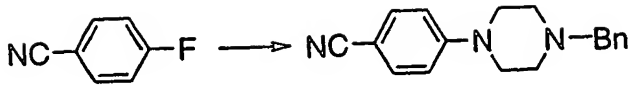
On page 26, replace the paragraph running from line 7 through line 9 with the following amended paragraph:

a) hydrogenation using a catalyst containing palladium, ~~platinium~~ platinum or nickel in a suitable solvent such as ethanol, methanol or acetic acid and at a reaction temperature between +20°C and +120°C or

On page 29, replace the paragraph running from line 13 through line 20 with the following amended paragraph:

(iii) Conversion of a compound of formula **XXXIII** to a compound

of formula **XXXIV**



XXXIII **XXXIV**

may be carried out by reaction with 1-benzylpiperazine in a suitable solvent such as *N,N*-dimethylformamide, dimethylsulfoxide or acetonitrile in the presence of a suitable base such as KOH or K_2CO_3 at a reaction temperature between +50°C and +150°C.

Replace the paragraph running from page 33, line 13 through page 34, line 2 with the following amended paragraph:

In the case when R_9 is C_1-C_6 alkyl or C_3-C_6 cycloalkyl the debenzylation is followed by the alkylation b) above using a suitable alkylation reagent such as R_1-Lg where Lg is a suitable leaving group, e.g., a halogen such as chlorine, bromine or iodine, or an alkane- or arenesulfonyloxy group such as a p-toluenesulfonyloxy group and R_1 is C_1-C_6 alkyl. The reaction may be carried out in a suitable solvent such as *N,N*-dimethylformamide, acetone, acetonitrile or tetrahydrofuran with a suitable base such as K_2CO_3, $NaHCO_3$, NaOH or a trialkylamine such as triethylamine. The reaction may be conducted at a temperature between +20°C and +120°C or, reductive alkylation

with a compound R_1-CHO, where R_1 is hydrogen or C_1-C_5 alkyl, or with a C_3-C_6 cyclic ketone, in the presence of a reductive agent such as sodium cyanoborohydride, sodium borohydride or catalytically with H_2 and a suitable catalyst containing palladium, ~~platinium~~ platinum, rhodium or nickel in a suitable solvent, e.g. tetrahydrofuran, dioxane, methanol or ethanol. A proton donor such as p-toluenesulfonic acid can be used to catalyze the formation of the imine/enamine and adjustment of pH to slightly acidic by an appropriate acid such as acetic acid may speed up the reaction.

Replace the heading of Example 33, lines 2 and 3 on page 53, with the following revised heading:

Example 33

(*S*)-*N*-[5-(4-Methylpiperazin-1-yl)-3,4-dihydro-2*H*-1-benzopyran-3-yl]-4-morpholinobenzenesulfonamide.

On page 61, replace the paragraph running from line 2 through line 13 with the following amended paragraph:

PHARMACOLOGY

Electrical field stimulation of [^{3}H]-5-HT release from occipital ~~cortex~~ cortices of guinea pigs

[^{3}H]-5-HT is released by electrical field stimulation from slices

of occipital ~~cortex~~ cortices of guinea pigs which have been pre-incubated with [^{3}H]-5-HT. This release is similar to that caused by nerve stimulation, i.e. exocytotic release from serotoninergic nerve terminals, depending on the presence of Ca^{2+} in the incubation medium. The 5-HT release is regulated at the level of the nerve terminals by autoreceptors, in the guinea pigs (like in humans) belonging to the h5-HT_{1B} receptor subtype. Thus, agonists of h5-HT_{1B} receptors reduce the amount of [^{3}H]-5-HT released by electrical field stimulation whereas the release is increased by antagonists of this receptor type. Testing compounds with this method is accordingly a convenient screening technique for determining the potency and functional effect of new h5-HT_{1B} receptor agonists and antagonists.

On page 61, replace the paragraph running from line 21 through line 29 with the following amended paragraph:

Preparation of occipital cortical slices

Guinea pigs (200-250g) were decapitated and the whole ~~brain was~~ brains were removed. The occipital ~~cortex was~~ cortices were dissected and cut to slices 0.4x4 mm with a McIlwain chopper machine. The white part of the tissue should be removed carefully with a tweezer before slicing. The slices were incubated in 5 ml buffer in the presence of 5 mM pargyline chloride. After incubation with 0.1 mM [^{3}H]-5-HT for another 30

min the slices were transferred to a test tube and washed three times with same volume buffer. The slices were transferred to the superfusion chambers with a plastic pipette and were washed for 40 min with the buffer in the presence of the uptake inhibitor citalopram at 2.5 μM with a flow rate of 0.5 ml/min.

Replace the **Results** section on page 62, lines 7 through 15, with the following amended section:

Results

A first electrical (or K^+) stimulation results in a standard amount of [^{3}H]-5-HT released (S_1). ~~Before~~ Between the first and the second stimulation the h5-HT_{1B} antagonist is added to the media, which results in a ~~dose depending~~ dose-dependent increase of the release (S_2) after the second stimulation. See Fig. 1.

The S_2/S_1 ratio, which is the per cent of released [^{3}H]-5-HT at the second stimulation (S_2) divided by that of the first stimulation (S_1), was used to estimate drug effects on transmitter release.